

PATENT COOPERATION TREATY

REC'D 08 JUL 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

29/09

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/NL2005/000216

International filing date (day/month/year)
22.03.2005

Priority date (day/month/year)
23.03.2004

International Patent Classification (IPC) or both national classification and IPC
C07K14/335

Applicant
WAGENINGEN CENTRE FOR FOOD SCIENCES

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/NL2005/000216

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☒ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/NL2005/000216

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-20
Inventive step (IS)	Yes: Claims	
	No: Claims	1-20
Industrial applicability (IA)	Yes: Claims	1-20
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following documents/:

- D1: KLEEREBEZEM MICHIEL ET AL: "Complete genome sequence of Lactobacillus plantarum WCFS1" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 100, no. 4, 18 February 2003 (2003-02-18), pages 1990-1995, XP002285325 ISSN: 0027-8424
- D2: DATABASE EMBL Cell Surface Protein 1 June 2003 (2003-06-01), XP002297276 retrieved from EBI Database accession no. Q88XH5
- D3: ADLERBERTH I ET AL: "A Mannose-Specific Adherence Mechanism in Lactobacillus plantarum Conferring Binding to the Human Colonic Cell Line HT-29" APPLIED AND ENVIRONMENTAL MICROBIOLOGY, WASHINGTON, DC, US, vol. 62, no. 7, July 1996 (1996-07), pages 2244-2251, XP002979206 ISSN: 0099-2240

Novelty, Article 33 (2) PCT.

D2 discloses a sequence which is 100% identical with SEQ ID NO. 1 of the application. Moreover, D1 discloses the whole genomic sequence of Lactobacillus plantarum of which the amino acid sequence presented in D2 is just one sequence. D1 discloses *inter alia* a nucleic acid sequence which is 100% identical to SEQ ID No. 2. However, no mention is made in either D1 or D2 of the ability of the peptide SEQ ID No.1 to bind mannose and act as a specific adhesin. This property is a function inherent of the sequence of the cell surface protein described in D2.

The consequence of the respective disclosures D1 and D2 is that all claims which pertain to sequences as product claims *per se* or methods which do not rely on the activity of adhesin as an essential feature are anticipated by these disclosures.

Inventive step, Article 33 (3) PCT

The Examining Division consider that D3 represents the closest prior art. D3 discloses a *Lactobacillus plantarum* strain displaying an ability to bind mannose coated beads. The authors speculate the existence of a mannose specific adhesin as a surface bound peptide receptor. No data is given as to the nature or sequence of this peptide. the objective problem is defined as;

"The cloning of a mannose specific adhesin in *Lactobacillus plantarum*"

The solution being the nucleic acid and peptide sequences SEQ ID Nos 2 and 1 respectively.

The application convincingly demonstrates that the peptide sequence SEQ ID No. 2 indeed possess the alleged activity and thus solves the objective problem, see pages 38-41.

Unfortunately for the Applicant this very sequences was known at the time of filing see D1 and D2 discussed above. However, although it is conceivable that second medical use claims and method claims relating exclusively to the unexpected finding that the known sequence from D1 and D2 is indeed a mannose specific adhesin would be allowable as presently claimed the claims do not meet the requirements of Article 33 (3) PCT.

Re Item VIII

Certain observations on the international application

Claim 1,2 and 11 relate to sequence "variants". This term is unclear and the skilled person does not know what is meant by such ambiguous nomenclature. As such said claims do not meet the requirements of Article 6 PCT. Furthermore, part © of claim 1 defines the nucleic acid for which protection is sought as a sequence which "hybridizes" the sequences claimed in part (a) or (b). Owing to the absence of conditions of stringency the sequences claimed are neither clear nor as they must possess the mannose binding activity supported in their breadth by the description.

Claim 16 is formulated as a method of treatment and as such does not conform with the

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AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/NL2005/000216

requirements for patentability in some PCT states for example in the regional phase it
contravenes Article 52 (4) EPC.